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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,614	05/08/2001	Yashwant M. Deo	MXI-166	4957

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LAHIVE & COCKFIELD, LLP
ONE POST OFFICE SQUARE
BOSTON, MA 02109-2127

EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/851,614	DEO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94 and 99-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *94 and 99-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-93 and 95-98 have been canceled.
Claims 94 and 99-107 are pending.

2. Applicant's amendment, remarks, and 1.132 declaration of Inventor Keler, submitted 9/29/06, are acknowledged.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 94 and 99-107 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) an isolated human monoclonal antibody, or antigen binding portion thereof, that binds to human dendritic cells, wherein the antibody comprises a human heavy chain variable region comprising FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 sequences and a human light chain variable region comprising FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 sequences, wherein the heavy chain CDR3 sequence comprises amino acid residues 99-105 of SEQ ID NO:4 or conservative sequence modifications thereof, and the light chain CDR3 sequence comprises amino acid residues 89-97 of SEQ ID NO:2 or conservative sequence modifications thereof (Claim 94),

B) the antibody of Claim 94 further comprising the limitations of Claims 95-98 and 100-107,

C) an isolated human monoclonal antibody, or antigen binding portion thereof, that binds to human dendritic cells, comprising a human heavy chain variable region comprising the amino acid sequence of SEQ ID NO:4, or conservative sequence modifications thereof and a human light chain variable region comprising the amino acid sequence of SEQ ID NO:2, or conservative sequence modifications thereof (Claim 94),

D) the antibody of Claim 99 further comprising the limitations of Claims 100-107.

Applicant argues that Claims 94 and 99 have been amended but offers no support. None has been found in the jumbo specification. Also note that Claim 99 has not been amended.

5. Claims 94 and 99-107 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

As set forth previously, Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of:

Any antibodies comprising "conservative modifications" of an antibody comprising SEQ ID NO:2 and SEQ ID NO:4, nor any antibodies, other than an antibody comprising SEQ ID NO"2 and SEQ ID NO:4, comprising the limitations of Claims 100-107.

The claims encompass a potentially unlimited genus of antibodies, just one of which has been disclosed, an antibody comprising SEQ ID NO:2 and SEQ ID NO:4. Given all of the possible "modified" antibodies of the claims, and all of the possible antibody fragments, i.e., antibody "portions", encompassed by the claims, the skilled artisan would conclude that the claimed genus would likely be large. Indeed, the skilled artisan would note that the claims further encompass antibodies comprising "modified portions" of the disclosed antibody. Accordingly, one of skill in the art would conclude that the specification fails to disclose a representative number of species, i.e., none save the antibody of SEQ ID NO:2 and SEQ ID NO:4, to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

Applicant's arguments, filed 9/29/06, have been fully considered but they are not persuasive. Applicant cites *Monsanto v. Mitchell*, 2006 U.S. App. LEXIS 20914 (Fed. Cir. August 16, 2006) and *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005) and argues, "Like the claims at issue in *Monsanto* and *Capon*, the present claims are drawn to antibodies having conservative modifications of particular variable region amino acid sequences and, thus, encompass modifications that are already known in the art. Accordingly, it is not necessary that they be described in the present specification".

It does not appear that the gene sequences in *Monsanto* and *Capon* comprised substitutions as do the antibody protein sequences in the instant case. It remains the Examiner's position that while substituted antibodies have been claimed,

none encompassed by the instant claims have been described in the instant specification nor in the prior art.

Applicant cites the 1.132 declaration of Inventor Keler.

A review of the declaration shows that the Inventor addresses the enablement rejection which is addressed by the Examiner below.

6. Claims 94 and 99-107 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth previously, With these teachings in mind, the instant specification would require a significant disclosure to enable the antibodies of the instant claims. In particular, the specification should demonstrate that the claimed antibodies, defined by as few as 2 CDR's (just 16 amino acid residues), further comprising "conservative sequence modifications", would function as claimed. Note that "conservative sequence modifications" is not defined in the specification, but, as the claims recite no limitations on the number of amino acids that can be "modified", it is clear that the claims encompass antibodies in which all of the amino acids are modified, i.e., amino acids that share 0% homology with the antibody comprising SEQ ID NOS:2 and 4. Looking to the specification for guidance, it is further noted that *no* examples of the claimed antibodies are disclosed. Additionally, it is noted that *no* examples of modified antibodies comprising the limitations of Claims 100-107 are disclosed.

While it may be possible to define an antibody by just its CDR3's, it is clear from the references submitted by Applicant that *at least* the CDR3's must be defined. Given that the instant specification provides no examples of the antibodies of the instant claims, other than B11, and given the fact that the specification does not even discuss any of the parameters and potential pitfalls of antibody engineering, one of ordinary skill in the art must conclude that the specification fails to adequately disclose how to make and use the claimed invention. Thus, the invention is considered to be highly unpredictable and requiring of undue experimentation to practice as claimed.

Applicant's arguments, filed 9/29/06, have been fully considered but they are not persuasive. Applicant argues "the claimed antibodies, and portions thereof, are limited to particular sequences and conservative modifications thereof, which represent a limited, art-recognized group of amino acid modifications. The antibodies must also retain their antigen binding function. Accordingly, the claims do indeed recite a clear limitation on the number of amino acids that can be modified".

While the art might recognize that the conservative modification of a single amino acid in a single CDR might not abrogate antigen binding, the art does not recognize that the modification of every amino acid in all 6 CDRs would not abrogate antigen binding. Such modified antibodies are encompassed by the instant claims.

Applicant cites the 1.132 declaration of Inventor Keler.

Inventor Keler opines that the modified antibodies of the instant claims are enabled. The Inventor cites multiple references in support of his opinion. The references are addressed here.

Brummell et al. (1993) describes experiments wherein individual site mutations are made in the heavy chain CDR3 of a well-known anti-*Salmonella* antibody. A review of the reference reveals that the particular antibody to be mutated was chosen because it was already well-defined and its crystal structure was known. Additionally, in describing a particular salt-bridge found in this antibody the authors state that, "In other antibodies, alterations to this salt-bridge gave *unpredictable* and interesting results" (emphasis added). Accordingly, it is the Examiner's position that simple, single, point mutations to this antibody teach little, if anything regarding the antibody of the instant claims comprising multiple substitutions.

Kobyashi et al (1999) describes experiments with an anti-DNA antibody. First note that similar to Brummell et al., the authors here make only single point mutations. More importantly, however, the authors study the electrostatic interactions of the DNA with the antibody. This then is not relevant to the antibody of the instant claims comprising multiple substitutions and (presumably) no electrostatic interactions.

Burks et al. (1997) describes an unusual antibody which the authors note, "Unlike other antibody-antigen complexes, binding does not appear to cause detectable conformational changes of either the antibody or the hapten. Both affinity and specificity are derived entirely from shape complementarity, since no hydrogen bonds have been identified between digoxin and the antibody". It appears then that studies with this antigen-antibody system cannot be applied generally to other antigen-antibody combinations. And again, the authors make only single point mutations and do not discuss the types of

antibodies of the instant claims wherein *every* residue in all 6 CDRs might be substituted..

Accordingly, it remains the Examiner's position that the instant specification offers only trial-and-error as a method for producing the claimed antibodies. Given no particular expectation of success that any particular modified construct would still bind human DCs, the production of the substituted antibodies of the instant claims is considered to comprise undue experimentation.

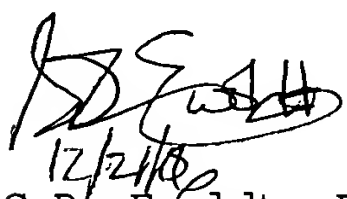
7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841..

10. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-

free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.



12/2/10

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600